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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/920,785	08/01/2001	Paul K. Nakane	266/106	5161

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EXAMINER
LILLING, HERBERT J

ART UNIT	PAPER NUMBER
1651	10

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/920,785	NAKANE, PAUL K.	
	Examiner	Art Unit	
	HERBERT J LILLING	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 21-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. Receipt is acknowledged of the amendment filed March 28, 2003.

2. Claims 1-16 and 21-22 are pending in this application.

Claims 17-20 have been cancelled.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 and 21-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention in view of the following:

a. The disclosure and claims are drawn to "nicotinamide diphosphate (NADP)" which does not correspond to the appropriate essential material for the histochemical reagent, see attachment whereby the essential material (NADP) does not match the name "nicotinamide diphosphate" does not match "NADP", see attachment Chem Abs Registry for NADP which does not match "nicotinamide diphosphate", see Registry page for NADP.

b. The statement in the specification for the only example on page 18, lines 5-6: which states the following:

" using methotrexate (Amethopterin), which is not a dihydrofolate reductase inhibitor"
and

lines 12-14: which states the following:

"were stained indicating that, as expected, methotrexate failed to inhibit dihydrofolate reductase, the biochemical pathway for which the histochemical reagent was designed was intact and TNBT was reduced to its colored form."

Methotrexate is a known dihydrofolate, which contradicts the statement in the specification, see Sigma Catalogue page 97.

Claims 1-15 and 21-22 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific example as disclosed on page 17 if Applicant can overcome the above rejections, in particular the nicotinamide diphosphate, does not reasonably provide enablement for the broad claimed inventions in view of the fact that the test will not give suitable results based on the claimed language. One of ordinary skilled in the art would obtain erroneous results based on the fact that the test depends upon the concentration of the reagents which may give a positive chromogenic test if the concentration of the antiobiotic is not sufficient to interact with the enzyme but the enzyme is still susceptible to the antibiotic. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and practice the invention commensurate in scope with these claims.

Claims 1-16 and 21-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention with respect to the comparative example as submitted on page 18 for Amethopterin which is a known potent inhibitor of dihydrofolate reductase, see Sigma Catalogue page 97 and that US 6316253 recite: " Cell lines that survive election with the appropriate toxin or antibiotic (e.g., methotrexate) have successfully undergone homologous.."

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7-8 and 21-22 are rejected under 35 U.S.C. 102(b) as anticipated by Watson et al U.S. 5,998,159.

Watson et al., anticipates the claimed inventions in view of the following disclosures which is within the scope of the claimed language for determining susceptibility of bacterial cells to an antiobiotic to form a test substrate that has been incubated to which is added a histochemical reagent that is capable of generating a chromogenic compound, see the following teachings in Watson et al:

For Broad Claim 1:

Column 1; lines 10-11 for "methods for high throughput screening for compounds with antibiotic activity".

Column 2, lines 33-34 "The compounds are then administered in conjunction with known antimicrobial agents. This technique is currently being tested for treating organisms resistant to tetracycline compounds"

Column 2, lines 45-67 drawn to sulonfamide antibiotics.

Columns 13-14, 19-22, column 24, line 54-column 26 and Examples column 29-column 31, line 42, anticipates the claimed inventions which employs a chromogenic compound to form a chromogenic color when the bacteria is not susceptible to antibiotics which disclosures are within the scope of the claimed inventions.

5. Claims 6 and 9-15 are rejected under 35 U.S.C. 103(a) as obvious over Watson et al U.S. 5,998,159 alone or further in view of Chen et al WO 99/18232

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The reference teaches in column 29 various bacteria that includes species within the scope of the claimed bacterial cells of claim 3, a synthetase, see column 20, line 24

within the scope of Claim 4; antibiotic tetracycline, see column 2, line 32 within the scope of claim 5; the use of ampicillin as an antibiotic, see column 23, line 4 and Watson et al teaches the use of visual means as well as conventional light meters to observe the color changes which renders claims 13 and 14 prima facie obvious to one of ordinary skilled in the art. The reference to Watson et al does not teach the biological samples which would have been prima facie obvious to one of ordinary skilled in the art to employ in view of the teaching of Chen et al to employ as the test samples feces or tissues, see page 13 in particular. In addition, Chen employs various fluorogenic as well as chromogenic substrates, which can be detected by various means, see pages 11 and 12. Chen also discloses essentially the same methods for determining the susceptibility of microorganisms to antibiotics.

6. **No claim is allowed.**

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Examiner Lilling whose telephone number is (703) 308-2034** and **Fax Number** is for applications **Before Final** (703) 872-9306 and **After Final** for applications is 703-872-9307 or SPE Michael Wityshyn whose telephone number is (703) 308-4743. Examiner can be reached Monday-Thursday from about 5:30 A.M. to about 3:00 P.M. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

H.J.Lilling: HJL
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Art Unit **1651**
June 02, 2003

Herbert J. Lilling

Dr. Herbert J. Lilling
Primary Examiner
Group 1600 Art Unit 1651